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EXAMINER	
SLOBODYANSKY,E	
ART UNIT	**PAPER NUMBER**
1652	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary

Application No.	Applicant(s)
09/430,029	Yano et al.
Examiner	**Group Art Unit**
Elizabeth Slobodyansky	1652

☒ Responsive to communication(s) filed on *Oct 29, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-55* is/are pending in the application.

Of the above, claim(s) *49-54* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-48, and 55* is/are rejected.

☒ Claim(s) *2* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The preliminary amendment filed concurrently with the specification amending claims 11 and 55 has been entered.

Claims 1-55 are pending.

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-48 and 55, drawn to a DNA encoding a toluene monooxygenase, a vector containing thereof, a cell transformed with the same, a method for producing of a toluene monooxygenase and methods of use of a transformed cell, classified in class 435, subclass 41.

II. Claims 49-54, drawn to a toluene monooxygenase, classified in class 435, subclass 189.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are patentably distinct because a DNA and a protein are different substances each with its own chemical structure and function, and they have different utilities. A DNA molecule of inventions I is not limited in use to the production of a toluene monooxygenase of invention II and can be used as a hybridization probe,

and a toluene monooxygenase of invention II can be obtained by a materially different method such as by the biochemical purification.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, fall into different statutory classes of invention, and are separately classified and searched, restriction for examination purposes as indicated is proper.

During a conversation with Mr. Lawrence Perry on September 26, 2000 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-48 and 55.

Affirmation of this election must be made by applicant in replying to this Office action. Claims 49-54 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The drawings filed concurrently with the application have been approved by Draftsman.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. 37 CFR 1.821(d) requires the use of assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences.

The following are examples of incompliance where sequence containing more than four amino acids or ten nucleotides are given without a sequence identifier: sequences recited on Figures 2, etc. There is no SEQ ID NO either on the figure or in the "Brief Description of Drawings".

Claim Objections

Claim 5 is objected to because of the following informalities. On line 3, it recites "replicate" where it appears "replicated" is intended.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6, 7, 9, 10, 15, 17, 19 and 55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 15 are directed to a genus of DNA fragment of 5.8 Kb with the specific restriction sites encoding any a toluene monooxygenase from any source. The specification teaches the structure of only a single representative species of such DNAs, a DNA fragment from *Burkholderia cepacia* KK01 (formerly, *Pseudomonas cepacia*). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding

a toluene monooxygenase. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 3, 9, 10, 17 and 55 recite sequences homologous to either amino acid or nucleic acid sequences or to otherwise variants of said sequences, i.e., having one or more deletion, substitution, and/or addition. This amounts to any structure having the same function as a protein encoded by SEQ ID NOs: 2-7 or a gene comprising SEQ ID NO:1. This is equivalent to a claim with no structural limitations wherein an enzyme or protein is defined by the function only.

The specification discloses no identifying characteristics which would allow to recognize a structure as a member of a gene encoding a toluene monooxygenase activity. Therefore, based on the instant disclosure, it is unpredictable either a protein is a part of a toluene monooxygenase and either a gene is a toluene monooxygenase gene. Thus, a toluene monooxygenase having an amino acid sequence homologous to SEQ ID NOs: 2-7 and a gene encoding said homologous sequence or a gene homologous to SEQ ID NO: 1, lack sufficient written description needed to practice the invention of claims 3, 9, 10, 17 and 55.

Claims 6, 7 and 19 recite a DNA fragment encoding a toluene monooxygenase comprising DNA sequences encoding ORFs of a gene encoding a toluene

monooxygenase. This is equivalent to claiming a gene by its coding regions only. The specification teaches one gene having the sequence of SEQ ID NO:1. The claims drawn to a gene encoding the amino acid sequence are insufficiently described in that a gene includes sequences in addition to the coding sequence such as promoters, introns, etc. The structure of these sequences is empirically determined . There is no known or disclosed correlation between the function of the gene and the structure of the non-described regulatory elements and untranslated regions of the gene. Therefore, one skilled in the art would not recognize from the disclosure that applicants were in possession of the genus of genes encoding a toluene monooxygenase at the time the invention was made.

Claims 1, 3, 6, 7, 9, 10, 15, 17, 19 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a toluene monooxygenase encoded by sequence of SEQ ID NO:1 and a DNA encoding SEQ ID NOs:2-7, does not reasonably provide enablement for a toluene monooxygenase a of an unknown amino acid sequence "homologous" to SEQ ID NOs:2-7 and a DNA encoding thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant invention is directed to a gene encoding a toluene monooxygenase having the sequence of SEQ ID NO:1. It comprises several coding regions encoding proteins of SEQ ID NOs:2-7. The above claims are drawn to sequences having structures different from SEQ ID NOS 2-7 or encoded by a modified SEQ ID NO:1 and retaining the requisite function.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any sequence that comprises SEQ ID NO:1 and encodes proteins of unknown structure obtained by deletion, substitution and/or addition from SEQ ID NOs:2-7 wherein said protein when aligned and linked in a certain order exhibit a toluene monooxygenase activity. This is because the specification does **not** establish: (a) regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of

such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, in order to make a toluene monooxygenase homologous to a toluene monooxygenase of the instant invention or a gene encoding thereof in a manner reasonably correlated with

the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 11, 17 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 17 are confusing because the relationship between a vector and a DNA fragment are unclear. For the sake of expedient prosecution, the examiner will interpret the claims as drawn to a vector comprising a DNA fragment.

Claims 11 and 55 are confusing because the relationship between a vector, a promoter and a DNA fragment are unclear. For the sake of expedient prosecution, the examiner will interpret the claims as drawn to a vector comprising a promoter operably linked to a DNA fragment.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

the claimed invention is directed to non-statutory subject matter.

Claims 1-3 and 6-10 recite "a DNA fragment". This reads on an entire organism that as a product of nature is unpatentable. Amending a claim to read "an isolated DNA" would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> a person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 9, 10 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Shields et al.

Shields et al. (US Patent 5,543,317, form PTO-1449) teach the enzyme having the same function as the enzyme of the instant invention. It is isolated from *Pseudomonas cepacia* $PR1_{23}$, i.e. from another strain of the same species. It is encoded by the sequence that is about 70% homologous to SEQ ID NO:1. As such the sequence of Shields et al. meets the limitation of a sequence having deletion, substitution and/or addition and as such anticipates claims 3, 9, 10 and 17.

Claims not specifically rejected in the above rejections are rejected as dependent on a rejected base claim.

Allowable Subject Matter

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

September 28, 2000